

General

Guideline Title

Revised guidelines for the diagnosis and management of hairy cell leukaemia and hairy cell leukaemia variant.

Bibliographic Source(s)

Jones G, Parry-Jones N, Wilkins B, Else M, Catovsky D, British Committee for Standards in Haematology. Revised guidelines for the diagnosis and management of hairy cell leukaemia and hairy cell leukaemia variant. *Br J Haematol.* 2012 Jan;156(2):186-95. [60 references]
[PubMed](#)

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: British Committee for Standards in Haematology. Guidelines on diagnosis and therapy. Hairy cell leukaemia. London (UK): British Committee for Standards in Haematology; 2000 Feb. 13 p.

Recommendations

Major Recommendations

Definitions for the quality of the evidence (A-C) and strength of recommendation (strong [grade 1], weak [grade 2]) are given at the end of the "Major Recommendations" field.

Clinical and Laboratory Features

- Blood film and bone marrow examination are essential for the diagnosis of hairy cell leukaemia (HCL). (Grade 1C)
- Flow cytometric evaluation should be undertaken when liquid material is available. CD-11c, CD25, CD103 and CD123 are advised if HCL is suspected. (Grade 1C)
- Immunohistochemistry on the marrow trephine specimens should include CD20 and DBA.44. (Grade 1C)
- CD20 is the most useful immunohistochemical stain to use when assessing remission status post-treatment. (Grade 1C)
- It is likely that screening for the presence of *BRAF* V600E mutation will be required in the near future. (Grade 2C)

Treatment

- Occasional patients who are asymptomatic may not require immediate therapy on diagnosis; active monitoring is appropriate. (Grade 2C)
- Patients with symptomatic cytopenia or painful splenomegaly require therapy. (Grade 1C)
- Purine analogues (cladribine or pentostatin) are the most appropriate agents for first-line therapy. No difference in efficacy between these two agents has been demonstrated. (Grade 1B)
- Subcutaneous cladribine administration is likely to be the most cost-effective option. (Grade 2C)

- Patients who have received cladribine or pentostatin who require transfusion should be transfused only with irradiated blood products for the rest of their lives in order to minimize the risk of transfusion-associated graft-versus-host disease. (Grade 1B)
- Patients who have received cladribine or pentostatin should receive aciclovir and co-trimoxazole prophylaxis for herpes reactivation and pneumocystis infection, respectively, until the lymphocyte count is $\geq 1 \times 10^9/l$. (Grade 2C)
- Patients who have received cladribine or pentostatin and have required treatment for herpes infections or pneumocystis should continue aciclovir or co-trimoxazole prophylaxis respectively until the CD4 count is $\geq 0.2 \times 10^9/l$. (Grade 2C)
- Response to purine analogue therapy should be assessed by bone marrow examination once the blood count has recovered, typically 4–6 months after cladribine therapy or after 8–9 courses of pentostatin. (Grade 1B)
- Residual disease should be treated using further purine analogue therapy. (Grade 2C)
- Eradication of minimal residual disease (MRD) (in contrast to overtly persistent disease) should not be the aim of therapy except as part of a clinical trial. (Grade 2C)
- Patients who relapse after purine analogue therapy should be re-treated either with the same or the alternative purine analogue depending upon the duration of remission. The use of rituximab is recommended in this setting. (Grade 2C)
- Routine use of growth factors is not recommended. (Grade 2C)
- Splenectomy can be considered if patients have symptomatic splenomegaly, particularly if marrow involvement is minimal. (Grade 2C)

Table. The Management of HCL

<p>Diagnosis: Bone marrow biopsy and abdominal CT essential</p> <p>Choice of therapy:</p> <ol style="list-style-type: none"> Most patients: Cladribine or pentostatin (see Table III in the original guideline document for regimens). Aim for CR Patients with large spleens and moderate or little BM involvement may have splenectomy first and nucleoside analogue therapy if/when evidence of progression <p>Choice of therapy at relapse: Either pentostatin or cladribine in combination with rituximab</p> <p>Monitor response: By BM trephine biopsy with immunocytochemistry (CD20, DBA.44) and abdominal CT (if previously abnormal)</p> <p>Prophylaxis: During lymphopenia: co-trimoxazole 960 mg three times per week; aciclovir (200 mg three times daily) may be indicated especially if there is a history of herpetic infection</p>
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HCL, hairy cell leukaemia; CT, computerized tomography; CR, complete remission; BM, bone marrow

Hairy Cell Leukaemia-Variant (HCL-v)

- It is not possible to make firm recommendations regarding the treatment of HCL-v; additional studies are required.
- Splenectomy results in partial remission for some patients. (Grade 2C)
- Purine analogues \pm rituximab may benefit some patients. (Grade 2C)

Definitions:

Quality of Evidence

(A) High: Further research is very unlikely to change confidence in the estimate of effect. Current evidence derived from randomized clinical trials without important limitations.

(B) Moderate: Further research may well have an important impact on confidence in the estimate of effect and may change the estimate. Current evidence derived from randomized clinical trials with important limitations (e.g., inconsistent results, imprecision – wide confidence intervals or methodological flaws – e.g., lack of blinding, large losses to follow up, failure to adhere to intention to treat analysis), or very strong evidence from observational studies or case series (e.g., large or very large and consistent estimates of the magnitude of a treatment effect or demonstration of a dose-response gradient).

(C) Low: Further research is likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate. Current

evidence from observational studies, case series, or just opinion.

Strength of Recommendations

Strong (grade 1): Strong recommendations (grade 1) are made when there is confidence that the benefits do or do not outweigh harm and burden. Grade 1 recommendations can be applied uniformly to most patients. Regard as 'recommend'.

Weak (grade 2): Where the magnitude of benefit or not is less certain a weaker grade 2 recommendation is made. Grade 2 recommendations require judicious application to individual patients. Regard as 'suggest'.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Hairy cell leukaemia
- Hairy cell leukaemia variant

Guideline Category

Diagnosis

Evaluation

Management

Treatment

Clinical Specialty

Hematology

Internal Medicine

Oncology

Intended Users

Physician Assistants

Physicians

Guideline Objective(s)

To provide healthcare professionals with clear guidance on the management of patients with hairy cell leukaemia (HCL)

Target Population

People in the United Kingdom who have or who are suspected to have hairy cell leukaemia or hairy cell leukaemia variant

Interventions and Practices Considered

Diagnosis/Evaluation

1. Blood film and bone marrow examination
2. Flow cytometry, if feasible, for CD11c, CD25, CD103, CD123
3. Immunohistochemistry of marrow trephine biopsy specimen for CD20 and DBA.44
4. CD20 immunohistochemistry to assess remission

Treatment/Management

1. Active monitoring without treatment
2. Purine analogue therapy (cladribine or pentostatin)
3. Purine analogues with or without rituximab for hairy cell variant
4. Transfusion with irradiated blood products (if transfusion is required)
5. Herpes prophylaxis with aciclovir
6. Pneumocystis prophylaxis with co-trimoxazole
7. Duration of prophylactic therapy
8. Timing of response assessment
9. Treatment of residual disease (eradication of minimal residual disease is not recommended)
10. Purine analogue therapy plus rituximab for relapsed disease
11. Splenectomy, as indicated

Note: The use of growth factors was considered and not recommended routinely.

Major Outcomes Considered

- Sensitivity and specificity of diagnostic tests
- Predictive value of prognostic tests
- Complete and partial remission rates
- Disease-free survival
- Event-free survival
- Overall survival
- Quality of life

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

MEDLINE and EMBASE were searched systematically for publications in English from 1990–2010 using key words: 'hairy cell leukaemia'.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence

The quality of evidence is graded as high (A), moderate (B) or low (C). To put this in context it is useful to consider the uncertainty of knowledge and whether further research could change what is known or is certain.

(A) High: Further research is very unlikely to change confidence in the estimate of effect. Current evidence derived from randomized clinical trials without important limitations.

(B) Moderate: Further research may well have an important impact on confidence in the estimate of effect and may change the estimate. Current evidence derived from randomized clinical trials with important limitations (e.g., inconsistent results, imprecision – wide confidence intervals or methodological flaws – e.g., lack of blinding, large losses to follow up, failure to adhere to intention to treat analysis), or very strong evidence from observational studies or case series (e.g., large or very large and consistent estimates of the magnitude of a treatment effect or demonstration of a dose-response gradient).

(C) Low: Further research is likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate. Current evidence from observational studies, case series, or just opinion.

Methods Used to Analyze the Evidence

Systematic Review

Description of the Methods Used to Analyze the Evidence

The 'GRADE' system (Grading of Recommendations Assessment, Development and Evaluation) was used to quote levels of evidence (see the "Rating Scheme for the Strength of Evidence" field).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The guideline group was selected to be representative of UK-based medical experts.

The writing group produced the draft guideline, which was subsequently revised with consensus by members of the Haemato-oncology Task Force of the British Committee for Standards in Haematology (BCSH).

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

Strong (grade 1): Strong recommendations (grade 1) are made when there is confidence that the benefits do or do not outweigh harm and burden. Grade 1 recommendations can be applied uniformly to most patients. Regard as 'recommend'.

Weak (grade 2): Where the magnitude of benefit or not is less certain a weaker grade 2 recommendation is made. Grade 2 recommendations require judicious application to individual patients. Regard as 'suggest'.

Cost Analysis

Subcutaneous cladribine administration is likely to be the most cost-effective option for management of hairy cell leukaemia (HCL) in pregnancy.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The guideline was reviewed by a sounding board of approximately 50 UK haematologists, the British Committee for Standards in Haematology (BCSH) and the British Society for Haematology Committee and comments incorporated where appropriate.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate diagnosis and management of hairy cell leukaemia (HCL)

Potential Harms

- Pentostatin requires a normal creatinine clearance (>60 ml/min) for the recommended dose but a half dose could be given if the clearance is between 40 and 60 ml/min. Anti-emetics should be given with each injection and prophylaxis with co-trimoxazole commenced when the patient becomes lymphopenic ($<1 \times 10^9/l$), continued for at least 6 months. Many units give a 1.5 litre intravenous fluid infusion with the drug to reduce renal toxicity.
- It is recommended that the use of concomitant drugs should be minimized during cladribine infusions as patients often develop rashes.
- Patients receiving pentostatin or cladribine should receive irradiated blood components indefinitely to prevent transfusion-associated graft-versus-host disease.

Qualifying Statements

Qualifying Statements

- The guidance presented in this guideline may not be appropriate to every patient with hairy cell leukaemia (HCL) and in all cases individual patient circumstances may dictate an alternative approach.
- While the advice and information in these guidelines is believed to be true and accurate at the time of going to press, neither the authors, the British Society for Haematology nor the publishers accept any legal responsibility for the content of these guidelines.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Safety

Identifying Information and Availability

Bibliographic Source(s)

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[PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2000 Feb (revised 2012 Jan)

Guideline Developer(s)

British Society for Haematology Guidelines - Professional Association

Source(s) of Funding

British Committee for Standards in Haematology

Guideline Committee

Haemato-oncology Thrombosis Task Force of the British Committee for Standards in Haematology

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Not stated

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Guideline Availability

Electronic copies: Available from the [British Committee for Standards in Haematology Web site](#) .

Print copies: Available from the British Committee for Standards in Haematology; Email: bcsh@b-s-h.org.uk.

Availability of Companion Documents

None available

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on July 30, 2012. The information was verified by the guideline developer on September 5, 2012. This summary was updated by ECRI Institute on November 21, 2013 following the U.S. Food and Drug Administration advisory on Arzerra (ofatumumab) and Rituxan (rituximab).

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